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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/446,089	12/17/1999	Keiko Sakakibara	001560-377	1763
7590	11/06/2002			
Ronald L Grudziecki Burns Doane Swecker & Mathis PO Box 1404 Alexandria, VA 22313-1404			EXAMINER EINSMANN, JULIET CAROLINE	
			ART UNIT	PAPER NUMBER

1634
DATE MAILED: 11/06/2002

326

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/446,089	SAKAKIBARA ET AL.	
	Examiner Juliet C Einsmann	Art Unit 1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) Responsive to communication(s) filed on 27 August 2002.
- 2a) This action is **FINAL**. 2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.
- 4) Claim(s) 1-9 and 18-26 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) Claim(s) _____ is/are allowed.
- 6) Claim(s) 1-9 and 18-26 is/are rejected.
- 7) Claim(s) 20 is/are objected to.
- 8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on _____ is/are: a) accepted or b) objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) The proposed drawing correction filed on _____ is: a) approved b) disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) All b) Some * c) None of:
1. Certified copies of the priority documents have been received.
2. Certified copies of the priority documents have been received in Application No. _____.
3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 14) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
a) The translation of the foreign language provisional application has been received.
- 15) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) Notice of References Cited (PTO-892)
2) Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____
- 4) Interview Summary (PTO-413) Paper No(s). _____
5) Notice of Informal Patent Application (PTO-152)
6) Other: _____

DETAILED ACTION

1. This action is written in response applicant's correspondence submitted August 27, 2002, paper number 35. Claims 1, 2, 4, 5, 7, 8, and 9 have been amended and claims 10-17 have been canceled, and claims 18-26 have been added. Claims 1-9 and 18-26 are pending. Applicant's amendments and arguments have been thoroughly reviewed, but are not persuasive for the reasons that follow. Any rejections not reiterated in this action have been withdrawn. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action. **This action is FINAL.**

2. Claim 20 is objected to because it recites "an amin oacid" in line 2 of the claim. Correction to "an amino acid" is required.

Claim Rejections - 35 USC § 112

3. Claims 1-9 and 18-26 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. MPEP 2163.06 notes "If new matter is added to the claims, the examiner should reject the claims under 35 U.S.C. 112, first paragraph - written description requirement. In re Rasmussen , 650 F.2d 1212, 211 USPQ 323 (CCPA 1981)."

In the instantly rejected claims, the new limitation of "preferentially using chalcones as substrates" in claims 1, 2, 4, 5, 18, 19, 20, 21, and 22 appears to represent new matter. No specific basis for this limitation was identified in the specification, nor did a review of the specification by the examiner find any basis for the limitation. Since no basis has been identified, the claims are rejected as incorporating new matter. The specification speaks

extensively about nucleic acids which have the ability to synthesize aurones using chalcones as substrates, but the specification does not particularly describe this activity as being directed towards any preferential substrate.

In claims 5 and 21, the use of the phrase "high stringency" appears to be new matter.

Although the specification at page 6 discusses a variety of stringency conditions, the specification does not indicate or discuss "high" stringency in particular. The word "high" is a relative term, and it is not discussed or defined in the specification.

4. Claims 1-9 and 18-26 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claims have been amended to include the language "preferentially using chalcones as substrates." However, the specification does not define what it means to "preferentially" use chalcones as a substrate, and thus, the metes and bounds of the claims are unclear.

Claims 5 and 21 are further indefinite over the recitation "high stringency." The word "high" is a relative term, and the specification does not provide any guidance as to which of the exemplified stringency conditions are high stringency conditions and which are low stringency conditions. Thus, the metes and bounds of the relative terminology cannot be determined.

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 1-9 and 18-26 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a nucleic acid encoding a protein having activity to

synthesize aureusidin by using chalcones as substrates, wherein the nucleic acid comprises a sequence encoding SEQ ID NO: 2, does not reasonably provide enablement for any other nucleic acids encoding such proteins, or for nucleic acids encoding proteins that have the ability to synthesize any other aurones. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Instant claim 1 encompasses gene which encodes a protein having activity to synthesize aurones by preferentially using chalcones as substrates. Claim 2 is drawn to an isolated gene obtained from a plant which encodes a protein having activity to synthesize aurones by preferentially using chalcones as substrates. Claims 3-5 each depend from claim one and recite that the claimed gene encodes SEQ ID NO: 2, or any amino acid sequence modified by deletion, substitution, and/or addition of one or more amino acids relative to SEQ ID NO: 2, or that the gene is hybridizes under high stringency to SEQ ID NO: 1, or that the encoded amino acid sequence has sequence homology to SEQ ID NO: 2, and encodes a protein having activity to synthesize aurones by preferentially using chalcones as substrates. Claims 6-9 recite vectors and host cells.

Claim 18 is drawn to an isolated nucleic acid encoding a protein having activity to synthesize aurones by preferentially using chalcones as substrates. Claim 19 is drawn to an isolated nucleic acid obtained from a plant which encodes a protein having activity to synthesize aurones by preferentially using chalcones as substrates. Claims 20-22 each depend from claim 18 and recite that the claimed gene encodes SEQ ID NO: 2, or any amino acid sequence modified by deletion, substitution, and/or addition of one or more amino acids relative to SEQ

ID NO: 2, or that the gene is hybridizes under high stringency to SEQ ID NO: 1, or that the encoded amino acid sequence has sequence homology to SEQ ID NO: 2, and encodes a protein having activity to synthesize aurones by preferentially using chalcones as substrates. Claims 23-26 recite vectors and host cells.

The specification teaches a single cDNA molecule (SEQ ID NO: 1) which encodes the polypeptide SEQ ID NO: 2. The working examples demonstrate that the polypeptide encoded by SEQ ID NO: 1 has the ability to synthesize aureusidin by using chalcones as substrates (Examples 3 and 6). The specification further teaches that the enzyme tyrosinase from the organisms Neurospora also has the ability to synthesize aureusidin by using chalcones as substrates (Example 18). The nucleic acid encoding the Neurospora tyrosinase was known in the prior art at the time the invention was made (see Kupper *et al.* and 102(b) rejections below), and by virtue of the fact that it was known in the prior art at the time the invention was made, this nucleic acid is also considered to be enabled by the prior art. Kupper *et al.* teach both the coding sequence of the Neurospora tyrosinase and the genomic sequence. The specification also teaches that instant SEQ ID NO: 2 has a copper binding region that is typical of the active center of polyphenol oxidases (Example 10).

The specification and the prior art are silent as to any other polypeptides that have the ability to synthesize aureusidin by using chalcones as substrates, or any polypeptides that have the ability to synthesize any other aurones (other than aureusidin) from chalcones. Neither the specification nor the prior art establish any relationship between all polyphenol oxidases and the activity that is attributed to instant SEQ ID NO: 2 and the Neurospora tyrosinase.

There are many polyphenol oxidase molecules (and nucleic acids encoding them) known in the prior art (see, for example, Hunt *et al.*, cited in paper number 30, Boss *et al.* and Robinson *et al.*, discussed below). However, neither the specification nor the prior art provide any guidance that would lead any person skilled in the art to select of all of the possibilities which nucleic acids already discovered, or yet to be discovered, would possess the ability to synthesize aureusidin by using chalcones as substrates, or the ability to synthesize any other aurone using chalcones as substrates. Particularly, the neither the specification nor the prior art provide any guidance as to which nucleic acids encoding polyphenol oxidase enzymes encode those that "preferentially" use chalcones as substrates. In fact the only common structural feature that the specification has suggested that instant SEQ ID NO: 2 has with polyphenol oxidases is the fact that it has a copper binding region.

While the level of skill in the relevant art is quite high (PhD in biochemistry), the level of unpredictability is higher with regard to the ability to change an amino acids in a particular sequence while still retaining the functionality of the enzyme. The specification provides absolutely no guidance as to which or how many of the amino acids of instant SEQ ID NO: 2 can be changed yet still result in a polypeptide which retains the ability to synthesize aureusidin by using chalcones as substrates, particularly by preferentially using chalcones as substrates. Further, the specification gives no guidance as to the structure or identity of nucleic acids encoding any other sequence that has the ability to synthesize aurones other than aureusidin.

The identification of other nucleic acids that fall within the scope of the instantly claimed invention would require the screening of every possible enzyme to determine if they have the recited functionality. Such a search would be complicated by the fact that the skilled artisan

would have no guidance as to which enzymes which are known or unknown would fall within the scope of the claimed invention.

Because of the breadth of the claims, the provision of only two sequences with the ability to synthesize aureusidin by using chalcones as substrates, the lack of any showing that other aurones could be synthesized, the fact that full length genes are not provided which encode polypeptides shown to have the ability to synthesize aureusidin by using chalcones as substrates, the lack of direction in the specification of the identity and structure of other such enzymes, and the large quantity of experimentation necessary to identify other members of the claimed group, it is concluded that undue experimentation would be necessary to practice the claimed invention commensurate in scope with the instantly rejected claims.

7. Claims 1-9 and 18-26 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Instant claim 1 encompasses gene which encodes a protein having activity to synthesize aurones by preferentially using chalcones as substrates. Claim 2 is drawn to an isolated gene obtained from a plant which encodes a protein having activity to synthesize aurones by preferentially using chalcones as substrates. Claims 3-5 each depend from claim one and recite that the claimed gene encodes SEQ ID NO: 2, or any amino acid sequence modified by deletion, substitution, and/or addition of one or more amino acids relative to SEQ ID NO: 2, or that the gene is hybridizes under high stringency to SEQ ID NO: 1, or that the encoded amino acid

sequence has sequence homology to SEQ ID NO: 2, and encodes a protein having activity to synthesize aurones by preferentially using chalcones as substrates. Claims 6-9 recite vectors and host cells.

Claim 18 is drawn to an isolated nucleic acid encoding a protein having activity to synthesize aurones by preferentially using chalcones as substrates. Claim 19 is drawn to an isolated nucleic acid obtained from a plant which encodes a protein having activity to synthesize aurones by preferentially using chalcones as substrates. Claims 20-22 each depend from claim 18 and recite that the claimed gene encodes SEQ ID NO: 2, or any amino acid sequence modified by deletion, substitution, and/or addition of one or more amino acids relative to SEQ ID NO: 2, or that the gene is hybridizes under high stringency to SEQ ID NO: 1, or that the encoded amino acid sequence has sequence homology to SEQ ID NO: 2, and encodes a protein having activity to synthesize aurones by preferentially using chalcones as substrates. Claims 23-26 recite vectors and host cells.

Claims 1 and 18 are so broad as to encompass nucleic acids encoding any possible enzyme that has the recited activity. The claim provides no structure to define the claimed nucleic acid. Claim 2 requires that the isolated gene or nucleic acid be obtained from a plant, but still, provides no structure to define the claimed invention. Claims 3 and 20 recite nucleic acids encoding SEQ ID NO: 2, but then allows that the nucleic acid can also encode a polypeptide modified by deletion, substitution, and/or addition of one or more amino acids relative to SEQ ID NO: 2, with no limit to the number of deletions, substitutions or additions. Essentially, the claims 3 and 20 provide no further structural limitation to the subject matter of claims 1 and 18 because claims 3 and 20 allow for an unlimited number of changes to the reference sequence.

Claims 4 and 21 encompass genes and nucleic acids that hybridize under high stringency conditions to SEQ ID NO: 1, yet the specification does not clearly define what encompasses high stringency conditions. This large genus is represented in the specification by one species, the nucleic acid encoding SEQ ID NO: 2. Thus, applicant is in possession of nucleic acids encoding only a single amino acid sequence, that is SEQ ID NO: 2.

The instant claims are also drawn to genes, and encompass, therefore, genomic coding sequences. Such a sequence includes 5' and 3' untranslated regions, introns, and other regulatory sequences. However, applicant has only described the coding portion of the nucleic acid encoding SEQ ID NO: 2.

As noted in the scope of enablement rejection, the specification does not teach a nucleic acid that has the ability to synthesize any aurone except aureusidin. With regard to the functional requirement of the claims, applicant is in possession only of nucleic acids encoding SEQ ID NO: 2 which has the activity to synthesize aureusidin from chalcones.

Thus, applicant has express possession of only one species in a genus which comprises hundreds of millions of different possibilities.

With regard to the written description, all of these claims encompass nucleic acid sequences different from those disclosed in the specific SEQ ID No:s which, for claims 5 and 21 includes modifications by permitted by the % identity language for which no written description is provided in the specification.

It is noted that in Fiers v. Sugano (25 USPQ2d, 1601), the Fed. Cir. concluded that

"...if inventor is unable to envision detailed chemical structure of DNA sequence coding for specific protein, as well as method of obtaining it, then conception is not achieved until reduction to practice has occurred, that is, until after gene has been

isolated...conception of any chemical substance, requires definition of that substance other than by its functional utility."

In the instant application, only nucleic acids encoding instant SEQ ID NO: 2 are described. Also, in Vas-Cath Inc. v. Mahurkar (19 USPQ2d 1111, CAFC 1991), it was concluded that:

"...applicant must also convey, with reasonable clarity to those skilled in art, that applicant, as of filing date sought, was in possession of invention, with invention being, for purposes of "written description" inquiry, whatever is presently claimed."

In the application at the time of filing, there is no record or description which would demonstrate conception of any nucleic acids that encode proteins modified by addition, insertion, deletion, substitution or inversion with respect to the disclosed SEQ ID No: 2 such that a different amino acid sequence is encoded which has the activity to synthesize aureusidin from chalcones.

Claim Rejections - 35 USC § 102

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) do not apply to the examination of this application as the application being examined was not (1) filed on or after November 29, 2000, or (2) voluntarily published under 35 U.S.C.

122(b). Therefore, this application is examined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

10. Claims 1, 2, 3, 4, 6, 7, 8, 18, 19, 20, 21, 23, 24, and 25 are rejected under 35 U.S.C. 102(b) as being anticipated by Kupper *et al.* (The Journal of Biological Chemistry, 1989, Vol. 264, No. 29, p. 17250-17258).

Kupper *et al.* teach a nucleic acid encoding a protein having activity to synthesize aurones by using chalcones as substrates. Specifically, Kupper *et al.* teach the gene encoding tyrosinase from Neurospora (Figure 7). This nucleic acid encodes a polypeptide that has the activity to synthesize aurones by using chalcones as substrates. The encoded polypeptide is an amino acid sequence modified by deletion, substitution, and/or addition of one or more amino acids relative to SEQ ID NO: 2. The polynucleotide taught by Kupper *et al.* is capable of hybridizing to instant SEQ ID NO: 1 under some stringency conditions. It is noted that the recitation of "high stringency" in claims 4 and 21 is indefinite for the reasons of record, so the relative term is being interpreted very broadly. Kupper *et al.* teach vectors comprising the nucleic acid encoding tyrosinase, as well as E.coli host cells transformed by such vectors (p. 17257).

It is noted that Kupper *et al.* do not teach that tyrosinase from Neurospora has the activity of synthesizing aurones by using chalcones, however, this ability is an inherent property of the tyrosinase whose gene is taught by Kupper *et al.* This functionality was in fact confirmed in Example 18 of the instant specification. Applicant is reminded that "The claiming of a new use, new function or unknown property which is inherently present in the prior art does not necessarily make the claim patentable (MPEP 2112)."

11. Claims 1-4, 6-9, 18-21, and 23-26 are rejected under 35 U.S.C. 102(e) as anticipated by Robinson (US 6242221).

Robinson teaches nucleic acids encoding polyphenol oxidases. The nucleic acid taught by Robinson as SEQ ID NO: 11 encodes a polypeptide having 64% local identity with instant SEQ ID NO: 2. The encoded polypeptide is an amino acid sequence modified by deletion, substitution, and/or addition of one or more amino acids relative to SEQ ID NO: 2. The polynucleotide taught by Kupper *et al.* is capable of hybridizing to instant SEQ ID NO: 1 under high stringency conditions because the nucleic acids have 64% local identity. Robinson does not teach that the polyphenol oxidase encoded by their SEQ ID NO: 11 has the activity to synthesize aurones from chalcones. However, the instant specification teaches that "enzymes having polyphenol oxidase activity clearly have activity to synthesize aurones by using chalcones as substrates (p. 8)." Because the nucleic acid taught by Robinson is a polyphenol oxidase, the nucleic acid taught by Robinson appears to be identical to the claimed nucleic acid. Robinson *et al.* further teach host cells from microorganisms and plants which are transformed by a vector comprising the polyphenol oxidase genes (Col. 9-10).

It is noted that this rejection has been withdrawn with respect to claims 5 and has not been applied to newly added claim 22 since the claims have been clarified and because Robinson does not teach a nucleic acid encoding a polypeptide having at least 55% homology over the entire length of the amino acid sequence SEQ ID NO: 2. The alignment of instant SEQ ID NO: 2 with the polypeptide taught by Robinson et al. has been attached to the instant action in order to provide a complete record.

12. Claims 1-4, 6-7, 9, 18-21, 23-24, and 26 are rejected under 35 U.S.C. 102(b) as anticipated by McBride *et al.* (WO 96/40951).

McBride *et al.* teach a nucleic acid encoding a protein having activity to synthesize aurones by using chalcones as substrates. Specifically, McBride *et al.* teach vectors comprising genes encoding tyrosinase and ORF438 from Streptomyces antibioticus (see p. 26, lines 18-29 and example 10). The encoded polypeptide is an amino acid sequence modified by deletion, substitution, and/or addition of one or more amino acids relative to SEQ ID NO: 2. The polynucleotide taught by McBride *et al.* is capable of hybridizing to instant SEQ ID NO: 1 under some stringency conditions. It is noted that the recitation of "high stringency" in claims 4 and 21 is indefinite for the reasons of record, so the relative term is being interpreted very broadly. McBride *et al.* teach vectors comprising the nucleic acid encoding tyrosinase, as well as E.coli and plant host cells transformed by such vectors (Example 11).

It is noted that McBride *et al.* do not teach that this tyrosinase from has the activity of synthesizing aurones by using chalcones, however, the polypeptide encoded by the nucleic acid taught by McBride *et al.* is a tyrosinase, and the instant specification teaches that at least one

tyrosinase meets the functional requirements of the instant claims. Furthermore, McBride *et al.* observed transgenic plants that exhibited an alteration in plant color (some meristem yellowing), which would result from the described activity (p. 56). Thus, the nucleic acid taught by McBride *et al.* appears to be identical to the claimed nucleic acid.

Response to Remark

112 1st, Scope of enablement

Applicant provides a quotation from the rejection wherein the examiner discusses the large quantity of experimentation necessary to identify other members of the claimed group, and asserts that this is not the proper standard for an enablement rejection. Quantity of experimentation, however, is one of the factors considered in the enablement inquiry. The following factors were considered in formulating the rejection contained herein (*In re Wands*, 858F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988): the breadth of the claims, the predictability or unpredictability of the art, the amount of direction or guidance presented, the presence or absence of working examples of the invention and the quantity of experimentation necessary. The examiner's conclusion that the quality of experimentation necessary to practice the claimed invention commensurate in scope with the breadth of the claims reaches the level of undue experimentation is based on an analysis all of the factors, as is evidenced by the discussion of each factor in the rejection.

Applicant argues that one skilled in the art would be able to practice the invention as claimed based upon the teachings of the specification using SEQ ID NO: 1 as a probe to obtain other sequence which could encode a protein having activity to synthesize aurones as instantly

claimed. However, this is not persuasive, because it is highly unpredictable, of all of the nucleic acids that would hybridize with instant SEQ ID NO: 1, which ones would have the ability to synthesize aurones by preferentially using chalcones as substrates. There is a complete lack of guidance in the specification as to how to select polynucleotides that encode enzymes having the ability to synthesize any aurone besides aurodesin. There is a compete lack of guidance as to how to select nucleic acids that encode enzymes that preferentially use chalcones as opposed to some other undefined substrate. The specification provides no guidance as to how SEQ ID NO: 2 can be modified while still arriving at a polypeptide with the recited activity. All of these are highly unpredictable areas, and absent further guidance the ordinary practitioner would not be able to practice the claimed invention commensurate in scope with the claims.

112 1st, Written description

Applicant asserts that the instant specification would describe the claimed genus to a person skilled in the art, presumable because the application describes how one skilled in the art could readily obtain additional genes and nucleotide sequences. However, this is not persuasive, because the issue is not COULD one obtain additional sequences, but instead, the issue is whether or not applicant had possession of the claimed invention at the time the invention was made or whether applicant adequately described the claimed invention to demonstrate such possession. In the instant application, the specification has demonstrated possession of a single nucleic acid molecule encoding a single polypeptide. The court has stated, "While we have no doubt a person so motivated would be enabled by the specification to make it, this is beside the point for the question is not whether he would be so enabled but whether the specification discloses the compound to him, specifically, as something appellants actually invented. We think

it does not." In Re Ruschig, 379 F.2d 990, 995, 154 U.S.P.Q. 118, 123 (CCPA 1967). Further, the court has stated "Accordingly, naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material."

The Regents of the University of California v. Eli Lilly & Co., 43 U.S.P.Q.2d 1406 (Federal Circuit 1997). In the instant case, it is not even clear that given the teachings of the specification one of skill in the art could in fact make the claimed invention. In either instance, the claimed invention does not meet the written description requirement for all of the reasons discussed herein.

With regard to claims 4 and 21, although these claims now recite "high stringency" hybridization conditions, the claims still do not meet the written description requirement, in light of the new amendments. First, the specification does not define the relative term "high stringency" as is suggested by applicant's arguments, but instead provides a series of exemplified stringency conditions, never designating which are high or low stringency conditions. Thus, the use of the term "high stringency" is not limiting in the way that applicant's arguments suggest. Further, the specification, while it teaches a method for screening enzymes for the ability to synthesize aurones from chalcones, does not describe how to identify the ones with "preferential" substrate specificity. Thus, this genus still does not meet the written description requirements.

Prior Art Rejections

Applicant argues that, unlike applicant's claimed gene, they tyrosinases of *Neurospora* origin have very broad substrate specificity, and that the enzymes of applicant's claimed

invention do not have tyrosinase activity. First, the claims do not exclude enzymes with tyrosinase activity, and further, it is unclear why it is relevant that instant SEQ ID NO: 2 does not have tyrosinase activity. Applicant's arguments for all three of the 102 rejections of record are based upon the fact that the enzymes of the present invention "preferentially" use chalcones as substrates, and the enzymes taught in the prior art do not. However, this assertion is unsupported by any evidence, and merely represents unsubstantiated attorney arguments. Arguments of counsel are not found to be persuasive in the absence of a factual showing. MPEP 716.01(c) makes clear that

"The arguments of counsel cannot take the place of evidence in the record. In re Schulze , 346 F.2d 600, 602, 145 USPQ 716, 718 (CCPA 1965). Examples of attorney statements which are not evidence and which must be supported by an appropriate affidavit or declaration include statements regarding unexpected results, commercial success, solution of a long - felt need, inoperability of the prior art, invention before the date of the reference, and allegations that the author(s) of the prior art derived the disclosed subject matter from the applicant."

Furthermore, it is not clear precisely what applicant means when referring to the fact that the claimed nucleic acids and genes encode polypeptides that "preferentially use chalcones as substrates" since such preferences are not described in the specification. On the other hand, the specification clearly demonstrates that the tyrosinase from Neurospora is able to use chalcones as substrates in the production of aureusidin. The specification specifically teaches that polyphenol oxidases have the functionality described in the specification as being the novelty of the instant invention. Thus, based on the teachings of the prior art and the specification, the nucleic acids in the prior art appear to be within the scope of the instant claims. Applicant is reminded that MPEP 2112.01 teaches "Where the claimed and prior art products are identical or substantially identical in structure or composition, or are produced by identical or substantially identical

processes, a prima facie case of either anticipation or obviousness has been established. In re Best, 562 F.2d 1252, 1255, 195 USPQ 430, 433 (CCPA 1977). ‘When the PTO shows a sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not.’”

Conclusion

13. No claims are allowed
14. A claim drawn to an isolated nucleic acid encoding SEQ ID NO: 2 would be free of the prior art and would be free of all of the other rejections of record.
15. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Juliet C. Einsmann whose telephone number is (703) 306-5824.

Application/Control Number: 09/446,089
Art Unit: 1634

Page 19

The examiner can normally be reached on Monday through Friday, from 9:00 AM until 4:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones can be reached on (703) 308-1152. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 and (703) 305-3014.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.



Juliet C Einsmann
Examiner
Art Unit 1634

November 4, 2002



JEFFREY FREDMAN
PRIMARY EXAMINER

Application/Control Number: 09/446,089
Art Unit: 1634

Page 20

SEQ ID NO: 12 of Robinson aligned against instant SEQ ID NO: 2.

Qy= instant SEQ ID NO: 2

Db= SEQ ID NO: 12 from Robinson

Query Match 23.9%; Score 713.5; DB 4; Length 196;
Best Local Similarity 63.8%; Pred. No. 2.2e-66;
Matches 127; Conservative 27; Mismatches 42; Indels 3; Gaps 2;

Qy 173 FFPFHRYYIYFFERILGKLINDTTFALQFWNYDSPGGMTIPSMFIDTNSSLYDSLRSNH 232
| | | | | : | : | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
Db 1 FLPFHRYYLYFYEKILGKLIGDETFAFPFWNWDAPGGMPMPSMYAKPSSPLYDELRAKH 60

Qy 233 QPPTIVDLNYAFSDSDNTTPEEQMIINLKIVYRQMVS SAKTPQLFFGRPYRRGDQEFPG 292
| | | | : | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
Db 61 QPPTLVLDLDYNFQDP--TNTDKQQIASNL SIMYRQVVSNGKTAQLFMGAAYRAGGEFDPG 118

Qy 293 VGSIELVPHGMIHLWTGSENTPYGENMGAFYSTARDPIFFAHHSNVDRMWSIWKTILGGPR 352
| | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
Db 119 AGSLENVPHGPVHIWTGDRTPNTEMGNFYSAARDPIFFAHHSNVDRMWSVWKTILGG-K 177

Qy 353 RTDLTDPDFLDASFVFYDE 371
| | | | | : | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
Db 178 RKDFTDPDWLNSGFLFYDE 196

SEQ ID NO: 11 of Robinson aligned against instant SEQ ID NO: 1.

Qy= instant SEQ ID NO: 1

Db= SEQ ID NO: 11 from Robinson

Query Match 11.9%; Score 233; DB 4; Length 590;
Best Local Similarity 64.3%; Pred. No. 1.4e-61;
Matches 385; Conservative 0; Mismatches 205; Indels 9; Gaps 2;

Qy 612 tttttcccggtccatagatattatctacttttgaaaaatattggaaaaactaatc 671
| | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
Db 1 tttttgcgttccatcgttactacacctacttctatgagaagatcttggcaagttgatt 60

Qy 672 aatgataacaactttgtctccaatttggaaactatgattcacctggtaatgacaatc 731
| | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
Db 61 ggagatgagacattgtctcccccttggaaactggatgcaccgggtggaatgccaatg 120

Qy 732 ccatcaatgttattgatactaattctcgctgtacgataggtaacggacagtaatcat 791
| | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
Db 121 ccgtccatgtacgccaaccatcgtcggcgtctacgacgagctgagagacgccaagcac 180

Qy 792 cagccaccaaccatcgtagacttgaactacgcctttctgattccgacaataccact 851
| | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
Db 181 cagccggcgcgtggatctggactacaactccaggatcccaccaacaccgaca-- 238

Qy 852 cctgaagagcaaatgattataaacctaaaattgtgtacagacaaatgtgtcgagcgct 911
| | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
Db 239 ----agcagcagatagccagcaacctctccatcatgtaccggcaggtggatgcgaatggc 294

SEQ ID NO: 11 of Robinson aligned against instant SEQ ID NO: 2 in a search for nucleic acids encoding instant SEQ ID NO: 2
Top line= instant SEQ ID NO: 2
Bottom line= SEQ ID NO: 11 of Robinson

alignment scores:

Quality: 713.50 Length: 199
Ratio: 4.197 Gaps: 2
Percent Similarity: 85.427 Percent Identity: 63.819

alignment block:

US-09-446-089D-2 x US-09-129-030-11 ..

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173 PhePheProPheHisArgTyrTyrIleTyrPhePheGluArgIleLeuG 189
|||:::||||||||||||||||:::||||||:::||||:::|||||||||||
1 TTTTGCGCTTCATCGTTACTACCTCTACTCTATGAGAAGATCTGGG 50

189 yLysLeuIleAsnAspThrThrPheAlaLeuGlnPheTrpAsnTyrAspS 206
||||||||:::||| ||||||||| - ||||||||:::|||:
51 CAAGTTGATTGGAGATGAGACATTGCTCTCCCCTCTGGAACTGGGATG 100

206 erProGlyGlyMetThrIleProSerMetPheIleAspThrAsnSerSer 222
::||||||||||| ::|||||||::: ::|||:
101 CACCGGGTGGAAATGCCAATGCCGTCCATGTACGCCAACCATCGTCGCCG 150

223 LeuTyrAspSerLeuArgAspSerAsnHisGlnProProThrIleValAs 239
||||||||:::|||||||:::|||||||:::|||||||:::|||||||:::|||||
151 CTCTACGACGAGCTGAGAGACGCCAAGCACCAGCCGCCACGCTGGTGG 200

239 pLeuAsnTyrAlaPheSerAspSerAsnThrThrThrProGluGluG 256

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Art Unit: 1634

||||::||| ||||::||| ||||::||| ::::::|
201 TCTGGACTACAACCTTCAGGATCCC.....ACCAACACCGACAAGCAGC 244

256 InMetIleIleAsnLeuLysIleValTyrArgGlnMetValSerSerAla 272
||::: |||||::|||:::|||::|||::|||::|||::|||::|||:
245 AGATAGGCCAGCAACCTCTCCATCATGTACCGGCAGGTGGTGTGAATGGC 294

273 LysThrProGlnLeuPhePheGlyArgProTyrArgArgGlyAspGlnG1 289
|||||| ||||||||::||| ||||||| ||| :::
295 AAGACGGCGCAGTTGTTCATGGGTGCGCGTAGAGAACGTGCCGCATGGGCCGGTCCATA 344

289 uPheProGlyValGlySerIleGluLeuValProHisGlyMetIleHisL 306
|||||||::|||::||| ||||||||| ::|||:
345 GGACCCCGGTGCCGGTCGCTAGAGAACGTGCCGCATGGGCCGGTCCATA 394

306 euTrpThrGlySerGluAsnThrProTyrGlyGluAsnMetGlyAlaPhe 322
::|||||||:::|||||: ||| ||||||||| |||
395 TCTGGACCGGTGACCGGACTCAGCCAACACGGAGAACATGGGAACTTC 444

323 TyrSerThrAlaArgAspProIlePhePheAlaHisHisSerAsnValAs 339
|||||||::| ||||||| ||||||| ||||||| |||||||
445 TACTCGCGGCAAGGGACCCGATCTTCTCGCCACCACCGAACGTCGA 494

339 pArgMetTrpSerIleTrpLysThrLeuGlyGlyProArgArgThrAspL 356
|||||||:::||| ||||||| ||||||| ::||| |||:
495 CCGGATGTGGAGCGTGTGGAAGACCCTGGGAGGG...AAGAGGAAGGACT 541

356 euThrAspProAspPheLeuAspAlaSerPheValPheTyrAspGlu 371
::|||||||:::|||:::|||:::|||||::|||:::|||||:
542 TCACTGACCCAGATTGGCTCAACTCGGGCTTCCTTCTACGACGAA 588